LETTERS TO THE EDITOR

Coagulation factor abnormalities after the Fontan procedure and its modifications

To the Editor:

Recently, the publication by Jahangiri and associates[1] suggested coagulation factor abnormalities, principally low levels of protein C, as contributing factors to thromboembolism in patients who underwent the Fontan operation.

They expressed the concentrations of the coagulant and anticoagulant factors as percentages of the concentration in pooled normal plasma set at 100%. Protein C was found to be below the normal range (63%-144%) in 15 of the 20 patients tested.

However, the ages of their patients ranged from 17 months to 13 years, whereas in normal children aged 1 to 5 years the mean value of protein C is 68% of the mean value of the pooled normal plasma (normal range 41%-95%).[2] In normal children aged 6 to 10 years, the mean value of protein C is 71% of the pooled normal plasma (normal range 46%-96%).[3] A significant proportion of their patients (±50%) were expected to have a value below the lower limit (63%), just because of their age and not because of their surgical condition. The same observation could probably explain partially the report of coagulation factor abnormalities after Fontan operations by Cromme-Dijkuis and associates.[4] In their publications, they compared protein C level in their patients (aged 4-23 years, median 10.5 years) with the normal ranges established in a group of 59 healthy volunteers, even though adults are probably the only ones to volunteer for plasma donation.

Before suggesting that a postoperative decrease of protein C should be regarded as a risk factor of thromboembolism after the Fontan operation, with the proposition to give anticoagulants, this study needs to be validated either with age-matched normal subjects or with the patients' values before surgery as control values.

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A word of caution in interpreting the ischemic time causing apoptosis in spinal cord ischemia

To the Editor:

We read with great interest the article titled "Delayed and Selective Motor Neuron Death After Transient Spinal Cord Ischemia: A Role of Apoptosis?" (J Thorac Cardiovasc Surg 1998;115:1310-5). The authors seemingly have shown apoptosis as the possible mechanism to explain late neuronal death in spinal cord ischemia. However, we would like to bring a few points to the attention of the readership:

1. There are some discrepancies between the text and Table I. The text *(Results: Neurologic outcome)* states that 4 rabbits (40%) were normal (grade 5) 2 days after the procedure (n = 10) and 4 rabbits (40%) had minimal ataxia (grade 4); however, according to Table I, grade 5 was observed in a total of 5 animals and grade 4 in only 3. Likely this was a typographic error.

2. In their results, no changes in systemic proximal aortic pressure were noted on inflation of the balloon catheter within the aorta below the renal arteries. In our experience in a rabbit model of abdominal aortic clamping via laparotomy, elevation of the blood pressure proximal to the clamp occurs universally, and this result is in agreement with both clinical observations and the physiologic principles.

3. In a model involving laparotomy, we have found a better correlation between esophageal and spinal cord temperature than between spinal cord and rectal temperature, which was their sole site of body temperature measurement. The normal rectal temperature of rabbits is usually between 38.3°C and 39.5°C. If rectal temperature is controlled at 37°C, that small temperature difference is enough to provide some degree of protection and to influence outcome.[1] In our experimental procedures the temperature of the heating pad was an important factor capable of influencing outcome, and that information is not provided in the paper. Were provisions made to avoid heating the paraspinal region?

4. Although we do not doubt the occurrence of the apoptotic phenomenon, the ischemic time of 15 minutes is questionable and should be taken cautiously. In our experience using volatile anesthetics (N_2O/O_2/isoflurane), 9 minutes of ischemia at an esophageal temperature of 38.5°C results in 60% recovery of function. However, with 10 or 11 minutes of ischemia only 20% of animals recovered function at 6 hours of reperfusion, paraplegia being apparent as early as 2 hours after reperfusion; none of the animals allowed to survive for 24 hours showed improvement if they had not recovered com-

pletely 6 hours after reperfusion.[2] In their study, 30% of animals subjected to 15 minutes of ischemia recovered function 8 hours after reperfusion, and 1 rabbit that had not recovered 24 hours after reperfusion did recover 2 days later. For 15 minutes of ischemia to result in 30% recovering acutely and 40% of animals recovering normal function when evaluated 2 days later, some sort of a protection (temperature or anesthetic factors, or a combination) must have taken place. Their anesthesia included ketamine (50 mg/kg), and ketamine is known to be an *N*-methyl-D-aspartate receptor antagonist, which in general promotes and facilitates hypothermia as part of its protective effects.[1,3,4] Since data obtained from experiments in which ketamine is used could not be extrapolated to the clinical situation, in which ketamine is not used, and because knowing the ischemic times when apoptosis starts to occur would be of clinical significance, the authors are encouraged to repeat their experiments without ketamine. We would suggest that they use volatile agents at concentrations that are not protective by themselves, rather than intravenous or intramuscular agents, and perhaps shorter ischemic times (6 and 7 minutes). Our prediction is that 7 minutes of ischemia at 38.5°C should result in a good number of animals showing apoptosis if seen 2 days after the ischemic episode. Also, although unlikely (since we believe apoptosis is a mechanism to get rid of injured elements), it would not be surprising if some of the animals with 6 minutes (so far found to recover completely within 6 hours of reperfusion) may prove to have apoptotic late neuronal death despite not having evidence of functional impairment when seen 6 hours after reperfusion.

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Reply to the Editor:

In our model, systemic proximal aortic pressure revealed only a trivial and transient change, not a significant change. Hence we believe that the change in proximal pressure has no influence on the spinal cord injury.

In this model spinal temperature was 37°C. Miyamoto and Miyamoto cited a reference that spinal cord temperature was more closely correlated with esophageal temperature. However, the correlation was not in the lumbar region but in the thoracic region, since the esophagus and lumbar region are at different levels. We believe esophageal temperature does not precisely reflect the lumbar spinal cord temperature. Therefore, we measured the temperature of the rectum, which is more proximal to the spinal cord in the lumbar region.

The models described by Miyamoto and Miyamoto are quite invasive. Previous reports describing spinal cord ischemia were made using laparotomy[1,2]; however, the aorta was occluded from 4 hours to 2 days after closure of the abdominal wall (the authors did not administer ketamine during the time the aorta was occluded). Therefore, their spinal ischemia model may not recover after 8 or 9 minutes of ischemia.

The word "apoptosis" describes histologic and biologic features.[3-6] However, in their letter, Miyamoto and Miyamoto have not described histologic and biologic findings in spinal cord ischemia.

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